DuPONT CENTRAL RESEARCH AND DEVELOPMENT
HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

November 4, 1993

MEMORANDUM

| TO : | | | |
|---|---|---|---|
| | M. S. BOGDANFFY | - CR&D | - HASKELL |
| | S. R. FRAME | - CR&D | - HASKELL |
| | M. E. HURTT | - CR&D | - HASKELL |
| | G. L. KENNEDY | - CR&D | - HASKELL |
| | N. D. KRIVANEK | - CR&D | - HASKELL |
| | C. F. REINHARDT, M.D. | - CR&D | - HASKELL |
| | V. L. REYNOLDS | - CR&D | - HASKELL |
| | E. D. RIEHL, M.D. | - CR&D | - HASKELL |
| | J. C. STADLER | - CR&D | - HASKELL |
| | H. J. TROCHIMOWICZ | - CR&D | - HASKELL |
| | J. F. VISKOCIL | - CR&D | - HASKELL |
| | J. WALRATH | - CR&D | - HASKELL |

FROM: R. C. GRAHAM, AEL COMMITTEE SECRETARY R.C. Graham

AEL COMMITTEE NOTES

Next Meeting - December 7, 1993
Starting At 9:00 a.m.
ROOM 619 HASKELL LABORATORY

1. Minutes of November 2, 1993 AEL Meeting

a. Decision Items

| | |
|---|---|
| CFC-113 [76-13-1] | $CEG_w$ = 10 mg/L |
| HCFC-123 [306-83-2] | $CEG_w$ = 3 mg/L |
| Isopar® E [64742-48-9] | AEL = 100 ppm (8- and 12-hour TWA) |

b. Finalization Items

| | |
|---|---|
| Chlorine [7782-50-5] | AEL = 0.5 ppm (8- and 12-hour TWA) |
| Dimethylformamide [68-12-2] | BEI = 20 ppm of MMF in an end-of-shift urine sample for several workers doing the same job and 40 ppm of MMF for an individual result |

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b. Finalization Items (Cont'd)

After discussion about the effect of hypoxia in an emergency situation, the time period for the FEEL for HFC-23 was reduced to 15 minutes.

| | |
|---|---|
| HFC-23<br>[75-46-7] | Fire Emergency Exposure Limit (FEEL) = 20% (v/v) for 2-15 minutes with a 23% (v/v) 1-minute ceiling concentration |

Other AEL List Items

AG requested the common name of the active ingredient in Fortress® Insecticide be changed from IN-43898 to chlorethoxyfos. Chlorethoxyfos will be added to the AEL List and also included in the Additions to the AEL List that are attached to these Notes.

It was brought to my attention that the ELC entry for benzene was incomplete. When benzene was reviewed in 1988, it was categorized as C 1988 and (D 1988). The (D 1988) categorization was never added to the AEL List. This will be corrected on the AEL List and also included in the Additions to the AEL List.

c. Discussion Items

Chromium Dioxide (Films) (S. R. Frame)

In a chronic inhalation study in rats, exposure to chromium dioxide produced lesions in the lungs similar to those produced by other dusts such as titanium dioxide and Kevlar® fibrils. In a 1982 IRDC report, these lesions were identified as squamous metaplasia in six females and squamous cell carcinomas in two females. As was recently done for Kevlar®, these lung lesions were re-examined by a panel of two Haskell pathologists and a non-DuPont consulting pathologist. They concluded that six of the eight lesions should be diagnosed as proliferative keratin cysts and the other two as squamous metaplasia. In the opinion of the pathologists conducting this re-examination, chromium dioxide was not carcinogenic in rats. No change in the current 0.1 mg/m$^3$ AEL is warranted. The hazard determination letter will be reissued.

Lenacil Herbicide (AG)

Lenacil, 3-cyclohexyl-6,7-dihydro-1H-cyclopentapyridine-2,4(3H,5H)-dione, has very low acute oral toxicity with an ALD in the rat of 11 g/kg. By skin absorption, lenacil has slight to very low toxicity with no deaths in rabbits administered 5000 mg/kg. When tested on the skin of guinea pigs, lenacil produced mild irritation at 10%, but no evidence of allergic skin sensitization. In the rabbit eye, lenacil powder produced mild conjunctival irritation. By the inhalation route, 5.2 mg/L of lenacil dust produced no deaths in rats exposed for 1-hour. In a chronic feeding study in rats, no oncogenic effect was observed and the only compound-related toxicity was a slight depression in growth and nutritional performance at the highest dose level (2500-10,000 ppm). In dogs, a 2-year administration of lenacil in their diet resulted in no compound-related toxicity. In a recently completed 18-month feeding study in mice, an increased incidence of hepatocellular adenomas occurred in the high-dose males. Lenacil was not mutagenic in the Ames test. Lenacil was not embryotoxic or teratogenic in pregnant rats and rabbits and had no effect on reproduction of rats.

Based on a NOAEL of 2500 ppm determined in the 18-month feeding study in mice, assuming a 70 kg worker body weight, inhalation of 10-15 $m^3$ of air during an 8-12 hour workday, and applying a safety factor, an AEL of 5 $mg/m^3$ (8- and 12-hour TWA), total dust was recommended. Also recommended was the consideration of an additional inhalation study (acute with histopathology of the respiratory tract).

2. Agenda for the December 7, 1993 AEL Meeting

a. Decision Items

| | |
|---|---|
| Lenacil [2164-08-1] | AEL = 5 $mg/m^3$ (8- and 12-hour TWA), total dust |

b. Finalization Items

| | |
|---|---|
| Refractory Aluminum Silicate Ceramic Fibers [142844-00-6] | AEL = 0.2 fibers/cc (Respirable fibers defined as less than 3 microns in diameter, greater than 5 microns in length, and with an aspect ratio of greater than 3:1), and 5 $mg/m^3$ (8-hour TWA) for non-fibrous particulate and/or non-respirable fiber |

c. Discussion Items

Ammonium Perfluorooctanoate (C-8) (Fluoropolymers)

Results from a 2-year mechanistic bioassay in rats with C-8 show increased incidences of combined hepatic adenomas, Leydig cell adenomas, and pancreatic acinar cell adenomas. In a previous bioassay, only the incidence of Leydig cell adenomas was increased. These data will be reviewed in light of the current 0.01 mg/m³ (8-hour TWA), skin AEL.

n-Hexane (Elastomers)

Data from a chronic inhalation study in mice show an increased incidence of liver tumors in females. No such increased tumor incidences occurred in male mice, nor in male or female rats. These data will be reviewed in light of the current 50 ppm (8- and 12-hour TWA) AEL.

Toluene (AP/Chemicals)

The German MAK was recently reduced from 100 ppm to 50 ppm and the the pregnancy classification changed to indicate that exposure at the 50 ppm MAK would present no risks for an unborn fetus. The data supporting the MAK and pregnancy classification will be reviewed in light of the developmental and reproductive toxicity data reviewed at the September AEL meeting. The need for a hazard determination letter will also be addressed.

IND-8556 and IN-70247 (AG)

These two intermediates, IND-8556 (N2,N2-dimethyl-6-(2,2,2-trifluoroethoxy)-1,3,5-triazine-2,4-diamine) and IN-70247 (methyl 2-(chlorosulfonyl)-3-methylbenzoate) are used in the synthesis of trisulfuron methyl, the active ingredient in a new sugarbeet herbicide. IND-8556 has slight acute oral toxicity with an ALD in the rat of 670 mg/kg. IND-8556 was negative in the Ames test. Two similar substituted triazine derivatives, IND-7556 (6-ethoxy-N4-methyl-1,3-5-triazine-2,4-diamine) and INL-5296 (N2,6-dimethyl-4-methoxy-1,3,5-triazine-2,4-diamine) have 1 mg/m³ AELs based on results from subchronic oral studies. IN-70247 has very low acute oral toxicity with an ALD in the rat of more than 11 g/kg. IN-70247 produced moderate skin irritation and mild ocular irritation in rabbits. In the Ames test, IN-70247 is negative. A similar compound, p-toluene-sulfonyl chloride has a 5 mg/m³ WEEL. AELs are requested for these two intermediates.

3. See pages 6-9 for the additions to the AEL List.

4. Items awaiting AEL Committee action are listed below.

AEL Committee Backlog of Requests

| Chemical Name | Business | Limit Requested |
|---|---|---|
| HCFC-124 | Fluorochemicals | FEEL |
| HFC-134a | Fluorochemicals | AEL |
| HFPO Trimer | Polymers | AEL |

Attendance at the November 2, 1993 Meeting

| Members | Guests |
|---|---|
| S. R. Frame | K. D. Barrowclough |
| M. E. Hurtt | W. J. Brock |
| G. L. Kennedy | S. L. Cattie |
| N. D. Krivanek | K. D. Dastur |
| C. F. Reinhardt, M.D. | G. S. Elliott |
| V. L. Reynolds | A. L. Grillo |
| E. D. Riehl, M.D. | D. P. Kelly |
| J. C. Stadler | J. E. Haase |
| H. J. Trochimowicz | D. E. Malek |
| J. F. Viskocil | S. P. Schmidt |
| J. Walrath | T. E. Slone |

Absent: M. S. Bogdanffy

## ADDITIONS TO THE AEL LIST**

| CHEMICAL [CAS#] | AEL | REMARKS | DATE FINAL/ STATUS | ELC GUIDELINES |
|---|---|---|---|---|
| Acrylic Acid [79-10-7] | 2 ppm | 8- and 12-hour TWA | 1993 | (C 1993)* (R 1993)* (D 1993)* (M 1993)* |
| Alkanol® XC Surfactant [68442-09-1] | 0.05 mg/m³ | 8- and 12-hour TWA | P1993 | |
| Benzene [71-43-2] | 1 ppm<br>5 ppm | 8- and 12-hour TWA<br>15-minute TWA | 1989 | C 1988 (D 1988)* |
| Boric Acid [10043-35-3] | 5 mg/m³ | 8- and 12-hour TWA | P1993 | |
| CFC-113 [76-13-1] | | $CEG_w$ = 10 mg/L | P1993 | |
| Chlorethoxyfos (Used in Fortress® Insecticide) [54593-83-8] | 0.05 mg/m³ (4 ppb) | 8-hour TWA, skin | 1990 | |
| Chlorine [7782-50-5] | 0.5 ppm | 8- and 12-hour TWA | 1993 | |
| Chloroform [67-66-3] | 2 ppm | 8- and 12-hour TWA | 1993 | c 1993 (D 1993)* (R 1993)* (M 1993)* |
| Cinmethylin (Used in Cinch® Herbicide) | | Not currently in use within DuPont. See the List of Inactive AELs for details. | | |
| 1,3-Dichloro-butene-2 [926-57-8] | 0.3 ppm | 8- and 12-hour TWA | 1993 | |

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* Substances or agents reviewed according to ELC Guidelines and not considered a carcinogenic, developmental, reproductive, or germ-cell mutagenic hazard are indicated by the appropriate letter within parentheses, e.g., (C), (D), (R), or (M).

** Last publication on April 8, 1993

## ADDITIONS TO THE AEL LIST**

| CHEMICAL [CAS#] | AEL | REMARKS | DATE FINAL/ STATUS | ELC GUIDELINES |
|---|---|---|---|---|
| Dimethylformamide [68-12-2] | | BEI = 20 ppm of MMF in an end-of-shift urine sample for several workers doing the same job and 40 ppm of MMF for an individual result | 1993 | (C 1993)* (D 1993)* (R 1993)* (M 1993)* |
| Diuron [330-54-1] | 1 mg/m³ | 8- and 12-hour TWA, total dust | 1993 | c 1993 (D 1993)* (R 1993)* |
| DPX-66037 [126535-15-7] | 2 mg/m³ | 8- and 12-hour TWA | P1993 | |
| Glutaraldehyde [111-30-8] | 0.03 ppm<br>0.1 ppm | 8-hour TWA<br>15-minute TWA | 1993 | |
| HCFC-123 [306-83-2] | 30 ppm | 8- and 12-hour TWA<br><br>$CEG_w$ = 3 mg/L | P1993 | |
| HFC-23 [75-46-7] | | FEEL = 20% (v/v) for 2-15 minutes with a 23% (v/v) 1-min. ceiling concentration | 1993 | |
| HFC-43-10 [138495-42-8] | 400 ppm | 8- and 12-hour TWA | 1992 | |
| INH-1044 [56-05-3] | 10 mg/m³ | 8-hour TWA, total dust | 1993 | |
| INJ-290 [36315-01-2] | 10 mg/m³ | 8-hour TWA, total dust | 1993 | |
| Isopar® E [64742-48-9] | 100 ppm | 8- and 12-hour | P1993 | |
| Isophthaloyl Chloride [99-63-8] | 0.5 ppm<br>1.0 ppm | 8- and 12-hour TWA<br>15-minute TWA | 1993 | |

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## ADDITIONS TO THE AEL LIST**

| CHEMICAL [CAS#] | AEL | REMARKS | DATE FINAL/ STATUS | ELC GUIDELINES |
|---|---|---|---|---|
| d-Limonene [5989-27-5] | 50 ppm | 8-hour TWA | 1993 | c 1989 (D 1989)* |
| Methylene Chloride [75-09-2] | 50 ppm<br>25 ppm | 8-hour TWA<br>12-hour TWA | 1993 | c 1993 (D 1993)* (R 1993)* |
| NER-010A [25038-04-4] | 0.1 mg/m³ | 8- and 12-hour TWA | 1993 | c 1993 |
| Nitrobenzene [98-95-3] | 0.1 ppm | 8- and 12-hour TWA, skin | 1993 | C 1993 r 1993 (D 1993)* |
| p-Nitrobenzoic Acid [62-23-7] | 2 mg/m³ | 8- and 12-hour TWA, skin | P1993 | c 1993 (R 1993)* |
| Oxalic Acid [144-62-7] | 1 mg/m³ | 8- and 12-hour TWA | P1993 | |
| n-Pentane [109-66-0] | 600 ppm | 8- and 12-hour TWA | 1993 | |
| m-Phenylenediamine [108-45-2] | 0.1 mg/m³ | 8- and 12-hour TWA | P1993 | |
| p-Phenylenediamine [106-50-3] | 0.1 mg/m³ | 8- and 12-hour TWA | P1993 | |
| p-Phenylene-diisocyanate (PPDI) [104-49-4] | 0.03 mg/m³ | 8- and 12-hour TWA, particulate and vapor combined | 1993 | |
| Propylene Glycol Monomethyl Ether Acetate [108-65-6] | 10 ppm | 8- and 12-hour TWA | 1992 | (D 1993)* |

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## ADDITIONS TO THE AEL LIST**

| CHEMICAL [CAS#] | AEL | REMARKS | DATE FINAL/ STATUS | ELC GUIDELINES |
|---|---|---|---|---|
| Refractory Aluminum Silicate Ceramic [142844-00-6] | 0.2 fibers/cc | 8- and 12-hour TWA; respirable fibers Fibers defined as < 3 microns in diameter, > 5 microns in length, and with an aspect ratio > 3:1 | P1993 | C 1993 |
| | 5 mg/m³ | 8-hour TWA for non-fibrous particulate and/or non-respirable fibers | | |
| SPN (Stripped 2-Pentenenitrile) | 0.3 ppm | 8- and 12-hour TWA, skin | P1993 | |
| Terephthaloyl Chloride [100-20-9] | 0.5 ppm | 8- and 12-hour TWA | 1993 | |
| | 1.0 ppm | 15-minute TWA | | |
| Trimethyl Phosphate [512-56-1] | 0.5 ppm | 8-hour TWA | 1992 | c 1993<br>R 1993<br>m 1993 |
| Ucon® 50-HB-660 [9038-95-3] | 0.5 mg/m³ | 8- and 12-hour TWA | 1993 | |
| Ucon® 50-HB-5100 [9038-95-3] | 0.01 mg/m³ | 8- and 12-hour TWA | 1993 | |

Richard C.. Graham
November 4, 1993
AEL27.20